

**PRELIMINARY AMENDMENT**  
Divisional of U.S. Appln. No. 09/210,578

**REMARKS**

The Amendments to the specification correct obvious typographical and clerical errors.

New claims 90-148 are supported by original claims 29-88. New claims 149-178 are supported by the original method claims, but recite that treatment occurs *ex vivo*. New claims 179-190 are supported by Examples 4, 5 and 6 at pages 25-26 of the specification.

Accordingly, no new matter is added. Entry and consideration of this Amendment is respectfully requested.

Respectfully submitted,

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**APPENDIX**

**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

**IN THE TITLE:**

Page 1, please delete lines 1-2 and insert therefore:

INTEGRATIVE PROTEIN-DNA COCHLEATE FORMULATIONS AND  
METHODS FOR TRANSFORMING CELLS

**IN THE SPECIFICATION:**

The specification is changed as follows:

**Page 11, paragraph encompassing lines 7-12:**

The individual lipid elements of the layered lipid bilayer of the cochleates precipitates can be any of the many known lipid structures having a negatively charged polar head group. Preferably the majority of the lipid elements of the lipid bilayer contain a negatively charged phospholipid headgroup. Upon contact with a lipid bilayer of a target cell, the layered lipid bilayer is capable of delivering one or more of the therapeutic nucleotide sequences and one or more AAV proteins to the interior of the target cell.

**Page 18, paragraph encompassing lines 13-16:**

Macroscopically, the final formulations consisted of heavy white suspensions. Phase contrast, light microscopic observation (1000x) indicated heavy suspensions of refractile granular crystals, ~~free and in aggregates in both free and aggregate form~~. Cochleate structure of the crystals was confirmed by addition of EDTA, which caused conversion of the cochleate crystals to liposomes.

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**Page 18, paragraph encompassing lines 18-23:**

Conditions to promote formation of DNA-binding protein complexes may vary but can be determined experimentally. Conditions used were TES buffer (100 mM NaCl, 2 ~~Mm~~-mM TES, 2 mM histidine, pH 7.4) at approximately 2 times the volume of protein in the buffer it was purified in (HEPES buffered, pH 7.5, 150 mM KCl, 1 mM MgCl<sub>2</sub>, 0.1 mM EDTA, and 10 mM maltose) using a ratio of DNA to lipid of 1.0:10.0 by weight. A probable range of useful ratios for formulations would be from 1:1 to 1:100 by weight.

**Page 21, in the Table, first line as follows:**

Neonatal blood cord blood CD34 <sup>+</sup> cells in 1 mg/ml G418	
Cochleate Type	Colonies/30 fields*
No Cochleates	20
CWRSVN Cochleates alone	23
CWRSVN Cochleates/Rep 68	26
CWRSVN Cochleates/Rep 78	27
CWRSVN Cochleates/Rep 68 and Rep 78	38

\*mean of duplicate plates

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Page 23, in the Table, last line as follows:

Neonatal cord blood CD34+ cells in 1.5 mg/ml G418		
	Colonies/30 Fields*	
Cochleate Type	Range	Mean
No cochleate	0	0
No cochleates/no G418	60-65	62
G1EN cochleate/Rep 68 & 78	0	0
CWRSVN cochleate alone	0-3	1.5 (sd 1.1)
G1EN retroviral vector**	1-2	1.4 (sd 0.2)
G1EN retroviral vector ***	16-26	18.3 (sd 5.4)
<del>SWRSVN</del> CWRSVN cochleate/Rep 68 & 78	2-8	5.25 (sd 2.2)

\* counted in quadruplicate plates

\*\* standard MMLV retroviral vector expressing neo resistance

\*\*\* transduced with cytokines for 3 days (standard retroviral  
transduction procedure)

IN THE CLAIMS:

Claims 1-88 are canceled.

Claims 89-139 are new.